

WHAT IS CLAIMED IS:

- A method of stimulating tear secretion and mucin production in eyes
 comprising the step of administering to the eyes an effective amount of a preparation which includes a compound selected from a group consisting of uridine 5'-triphosphate and derivatives as depicted in Formula I, dinucleotides as depicted in Formulae II, II(a) and II(b), adenosine 5'-triphosphate derivatives as depicted in Formula III, and cytidine 5'-triphosphate derivatives as depicted in Formula IV, and their pharmaceutically
 acceptable salts; and
 - a physiologically compatible vehicle selected from the group consisting of aqueous electrolyte solutions, polyethers, polyvinyls, polymers of acrylic acid, lanolin, and glucosaminoglycans;
 - whereby said preparation promotes tear secretion and mucin production in the eyes in a subject in need of such treatment:

FORMULA I

wherein:

 X_1 , X_2 and X_3 are each independently either O or S;

20 R₁ is O, imido, methylene or dihalomethylene; R₂ is H or Br;

FORMULA II

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wherein:

X is oxygen, imido, methylene or difluoromethylene;

$$n = 0 \text{ or } 1;$$

$$m = 0 \text{ or } 1;$$

$$n + m = 0$$
, 1 or 2; and

B and B' are each independently a purine residue, as in Formula IIa, or a pyrimidine residue, as in Formula IIb, linked through the 9- or 1-position, respectively:

FORMULA IIa

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$$R_3$$
 R_1
 R_1
 R_2
 R_3
 R_3
 R_4
 R_2
 R_3
 R_4
 R_4
 R_5
 R_4
 R_5
 R_7
 R_7
 R_8
 R_9
 R_9

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wherein:

 R_3 is NHR₁;

 R_1 of the 6- or 8-HNR₁ groups is chosen from the group consisting of hydrogen, arylalkyl (C_{1-6}) groups; and alkyl groups with functional groups selected from the group consisting of ([6-aminohexyl]carbamoylmethyl)-, ω -acylated-amino(hydroxy, thiol or carboxy)alkyl(C_{2-10})- and ω -acylated-amino (hydroxy, thiol or carboxy) derivatives where

the acyl group is chosen from the group consisting of acetyl, trifluroacetyl, benzoyl, and substituted-benzoyl;

FORMULA IIb

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$$R_7$$
 R_6
 A_5
 A_5
 A_6
 A_5
 A_6
 A_6

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wherein:

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 R_4 is hydroxy, mercapto, amino, cyano, aralkoxy, C_{1-6} alkoxy, C_{1-6} alkylamino or dialkylamino, with the alkyl groups optionally linked to form a heterocycle;

 R_5 is hydrogen, acyl, C_{1-6} alkyl, aroyl, C_{1-5} alkanoyl, benzoyl, or sulphonate;

 R_6 is hydroxy, mercapto, alkoxy, aralkoxy, C_{1-6} -alkylthio, C_{1-5} disubstituted amino, triazolyl, alkylamino or dialkylamino, where the alkyl groups are optionally linked to form a heterocycle or linked to N^3 to form an optionally substituted ring;

R₇ is hydrogen, hydroxy, cyano, nitro, alkenyl with the alkenyl moiety optionally linked through oxygen to form a ring optionally substituted on the carbon adjacent to the oxygen with alkyl or aryl groups, substituted alkynyl, halogen, alkyl, substituted alkyl, perhalomethyl, C₂₋₆ alkyl, C₂₋₃ alkenyl, or substituted ethenyl, C₂₋₃ alkynyl or substituted alkynyl;

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or together $R_6 - R_7$ form a 5 or 6-membered saturated or unsaturated ring bonded through N or O at R_6 , such a ring optionally contains substituents that themselves contain functionalities; provided that when R_8 is amino or substituted amino, R_7 is hydrogen; and

R₈ is hydrogen, alkoxy, arylalkoxy, alkylthio, arylalkylthio, carboxamidomethyl, carboxymethyl, methoxy, methylthio, phenoxy or phenylthio;

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wherein:

 R_1 , X_1 , X_2 and X_3 are defined as in Formula I;

 R_3 and R_4 are H while R_2 is nothing and there is a double bond between N-1 and C-6, or

R₃ and R₄ are H while R₂ is O and there is a double bond between N-1 and C-6, or R₃, R₄ and R₂ taken together are -CH=CH-, forming a ring from N-6 to N-1 with a double bond between N-6 and C-6;

FORMULA IV

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wherein:

 R_1 , X_1 , X_2 and X_3 are defined as in Formula I;

 R_5 and R_6 are H while R_7 is nothing and there is a double bond between N-3 and C-4, or

R₅, R₆ and R₇ taken together are -CH=CH-, forming a ring from N-3 to N-4 with a double bond between N-4 and C-4 optionally substituted at the 4- or 5-position of the etheno ring.

- 2. A method according to Claim 1, wherein said administration involves topical administration of said compound via a carrier vehicle selected from a group consisting of drops of liquid, liquid wash, gels, ointments, sprays and liposomes.
- 3. A method according to Claim 2, wherein said topical administration comprises infusion of said compound to said ocular surface via a device selected from a group consisting of a pump-catheter system, a continuous or selective release device, and a contact lens.
- 4. A method according to Claim 1, wherein said administration involves systemic administration of said compound by administering a liquid/liquid suspension of said compound via nose drops or nasal spray or nebulized liquid to oral or nasopharyngeal airways of said subject, such that a therapeutically effective amount of said compound contacts the lacrimal tissues of said subject via systemic absorption and circulation.
- 5. A method according to claim 1, wherein said systemic administration of said compound is accomplished by administering an oral form of said compound, such that a therapeutically effective amount of said compound contacts the lacrimal tissues of said subject via systemic absorption and circulation.
- 6. A method according to claim 4, wherein said systemic administration of said compound is accomplished by administering an injectable form of said compound, such that a therapeutically effective amount of said compound contacts the lacrimal tissues of said subject via systemic absorption and circulation.
- 7. A method according to claim 4, wherein said systemic administration of said compound is accomplished by administering a suppository form of said compound,

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such that a therapeutically effective amount of said compound contacts the lacrimal tissues of said subject via systemic absorption and circulation.

- 8. A method according to claim 4, wherein said systemic administration of said compound is accomplished by administering an intra-operative instillation of a gel, cream, powder, foam, crystals, liposomes, spray or liquid suspension form of said compound, such that a therapeutically effective amount of said compound contacts the lacrimal tissues of said subject via systemic absorption and circulation.
- 9. A method according to Claim 1, wherein said compound is administered in an amount sufficient to achieve concentrations thereof on the ocular surfaces of said subject of from about 10⁻⁷ to about 10⁻¹ moles/liter.
 - 10. A method of stimulating tear secretion and mucin production in eyes comprising the step of administering to the eyes an effective amount of P¹, P⁴-di(uridine-5')-tetraphosphate.
 - 11. A method of treating dry eye diseases comprising the step of administering to the eyes an effective amount of P¹, P⁴-di(uridine-5')-tetraphosphate.
 - 12. A method of treating corneal injury comprising the step of administering to the eyes an effective amount of P¹, P⁴-di(uridine-5')-tetraphosphate.

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